10/017,577 LYCOOK 12/7/04

d his

(FILE 'HOME' ENTERED AT 12:15:04 ON 07 DEC 2004)

	FILE 'BIOS	IS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT	
	12:15:23 O	N 07 DEC 2004	
L1	2581	S (ENZYME CONJUGATE)	
L2	472	S L1 AND DRUG?	
L3	378	S L2 AND ANTIBOD?	
L4	0	S L3 AND ARRAY?	
L5	24	S L3 AND IMMOBILI?	
L6	22	DUPLICATE REMOVE L5 (2 DUPLICATES REMOVED)	
T.7	6	S L1 AND COCAINE?	

4 DUPLICATE REMOVE L7 (2 DUPLICATES REMOVED)

=>

```
1992:190639 CAPLUS
AN
     116:190639
DN
     Entered STN: 16 May 1992
ED
     An analyte-substitute reagent for use in specific binding assay methods,
ΤI
     devices and kits
     Baugher, Bennett W.; Devereaux, Sharon M.; Chamberlain, Aurora J.;
IN
     Ungemach, Frank S.
     Abbott Laboratories, USA
PA
     Eur. Pat. Appl., 19 pp.
SO
     CODEN: EPXXDW
DT
     Patent
     English
LΑ
IC
     ICM G01N033-53
     ICS G01N033-543
     9-10 (Biochemical Methods)
     Section cross-reference(s): 4, 23, 24, 25
FAN.CNT 1
                         KIND
                                  DATE
                                              APPLICATION NO. DATE
     PATENT NO.
     EP 467078
                          A2
                                  19920122 EP 1991-109936
                                                                     19910618
PΙ
     EP 467078
                          A3 19920506
     EP 467078
                          В1
                                19960508
         R: DE, ES, FR, IT
ES 2089057 T3 19961001 ES 1991-109936
CA 2047050 AA 19920119 CA 1991-2047050
JP 04232860 A2 19920821 JP 1991-178035
JP 2579392 B2 19970205
US 5340748 A 19940823 US 1993-67254
US 5501985 A 19960326 US 1994-230995
PRAI US 1990-554304 A 19900718
US 1993-67254 A1 19930525
                                                                       19910618
                                                                       19910715
                                                                       19910718
                                                                      19930525
                                                                     19940421
CLASS .
               CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                 ____
                ICM G01N033-53
 EP 467078
                 ICS
                         G01N033-543
 EP 467078 ECLA G01N033/543B; G01N033/94
US 5501985 ECLA G01N033/543B; G01N033/94H
     Reagents, devices, methods, and kits used in the anal. of low-mol.-weight
AB
     compds. too small to bind 2 sp.-binding members at the same time are
     described. The method comprises (a) contacting the test sample
     sequentially or simultaneously with (i) an analyte-substitute reagent
     comprising an analyte component attached to a ligand component and (ii) a
     1st sp. binding member capable of binding an epitope on both the test
     analyte and the analyte component; (b) contacting mixture from a
     sequentially or simultaneously with (i) a capture reagent comprising a 2nd
     binding member sp. for the analyte-substitute reagent and (ii) an
     indicator reagent comprising a label and a 3rd binding member for binding
     the reagent; and (c)detecting bound or free label. The analyte component
     has ≥1 epitope in common with the analyte, and the ligand component
     binds to a ligand-binding member but is not reactive with the analyte-sp.
     binding member. A competitive EIA for cocaine in urine is
     described using antibody to a cocaine analog (preparation described)
     (I), a I-fluorescein derivative complex as the analyte-substitute reagent, and
     antifluorescein antibody capture reagent conjugated to latex
     microparticles.
ST
     small analyte specific binding assay; immunoassay small analyte;
     competitive immunoassay small analyte; cocaine competitive EIA;
     enzyme immunoassay cocaine
IT
        (carboxy-derivatized, microparticles, conjugates with anti-fluorescein
```

ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

```
antibody, for cocaine immunoassay)
ΙT
     Surfactants
        (effect of, in morphine immunoassay)
ΙT
     Immunoassay
        (of low-mol.weight analyte, analyte-substitute reagents for)
IT
     Antibodies
     RL: ANST (Analytical study)
        (to cocaine analog, enzyme conjugates, in
        cocaine immunoassay)
IT
     Immunoassay
        (competitive, of low-mol.weight analyte, analyte-substitute reagents for)
IT
     Albumins, compounds
     RL: ANST (Analytical study)
        (conjugates, with cocaine analog, as immunogen for
        cocaine-reactive antibodies)
IT
     Thyroglobulins
     RL: ANST (Analytical study)
        (conjugates, with morphine analog, in morphine immunoassay)
     2321-07-5, Fluorescein
     RL: ANST (Analytical study)
        (antibodies to, in cocaine immunoassay)
TТ
     20290-09-9D, thyroglobulin conjugates
     RL: ANST (Analytical study)
        (as immunogen for antibodies to morphine)
IT
     57-27-2, Morphine, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (determination of, by immunoassay)
IT
     50-36-2, Cocaine
     RL: ANT (Analyte); ANST (Analytical study)
        (determination of, in urine, by competitive EIA)
IT
     140457-30-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and amination of, in cocaine analog preparation for
        immunoassay)
ΙT
     119094-47-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and amination of, in preparation of reagent for morphine
        immunoassay)
IT
     5796-31-6P, Ecgonine hydrochloride
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and esterification of, in cocaine analog preparation for
        immunoassay)
IT
     119094-63-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrogenation of, in preparation of reagent for morphine
        immunoassay)
     140457-34-7P
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, as cocaine analog for immunoassay)
     7143-09-1P, Ecgonine methyl ester 140457-31-4P
                                                         140457-32-5P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, in cocaine analog preparation for
        immunoassay)
ΙT
     140457-34-7DP, albumin conjugates
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as immunogen, for preparation of antibodies reactive with
```

```
cocaine)
     82169-58-2DP, reaction products with morphine derivative 140476-25-1DP,
IT
     reaction products with fluorescein derivative
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as reagent in morphine immunoassay)
IT
     140476-25-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, in preparation of reagent for morphine immunoassay)
     34619-03-9, Di-tert-butylcarbonate
IT
     RL: ANST (Analytical study)
        (reaction of with cocaine analog, in cocaine analog
        preparation for immunoassay)
IT
     9001-78-9D, conjugates with antibodies
     RL: ANST (Analytical study)
        (to cocaine analog, for cocaine immunoassay)
     9003-53-6D, Polystyrene, conjugates with antibodies
     RL: ANST (Analytical study)
        (to fluorescein, in morphine immunoassay)
     51306-35-5D, complexes
IT
     RL: ANST (Analytical study)
        (with cocaine analog, as reagent for cocaine
        immunoassay)
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     Eur. Pat. Appl., 19 pp.
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     CODEN: EPXXDW
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     Patent
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     ICM G01N033-53
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     9-10 (Biochemical Methods)
     Section cross-reference(s): 4, 23, 24, 25
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                                  19920506
         R: DE, ES, FR, IT
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US 5501985 A 19960326
PRAI US 1990-554304 A 19900718
US 1993-67254 A1 19930525
                               19961001 ES 1991-109936
19920119 CA 1991-2047050
19920821 JP 1991-178035
                                                                       19910618
                                                                        19910715
                                                                       19910718
                                  19940823 US 1993-67254
19960326 US 1994-230995
                                                                       19930525
CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
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                ICM
                         G01N033-53
                 ICS
                         G01N033-543
 EP 467078 ECLA G01N033/543B; G01N033/94 US 5501985 ECLA G01N033/543B; G01N033/94H
     Reagents, devices, methods, and kits used in the anal. of low-mol.-weight
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     analyte and the analyte component; (b) contacting mixture from a
     sequentially or simultaneously with (i) a capture reagent comprising a 2nd
     binding member sp. for the analyte-substitute reagent and (ii) an
     indicator reagent comprising a label and a 3rd binding member for binding
     the reagent; and (c)detecting bound or free label. The analyte component
     has ≥1 epitope in common with the analyte, and the ligand component
     binds to a ligand-binding member but is not reactive with the analyte-sp.
     binding member. A competitive EIA for cocaine in urine is
     described using antibody to a cocaine analog (preparation described)
     (I), a I-fluorescein derivative complex as the analyte-substitute reagent, and
     antifluorescein antibody capture reagent conjugated to latex
ST
     small analyte specific binding assay; immunoassay small analyte;
     competitive immunoassay small analyte; cocaine competitive EIA;
     enzyme immunoassay cocaine
     Latex
IT
```

(carboxy-derivatized, microparticles, conjugates with anti-fluorescein

ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

```
antibody, for cocaine immunoassay)
IT
     Surfactants
        (effect of, in morphine immunoassay)
IT
     Immunoassay
        (of low-mol.weight analyte, analyte-substitute reagents for)
ΙT
     Antibodies
     RL: ANST (Analytical study)
        (to cocaine analog, enzyme conjugates, in
        cocaine immunoassay)
ΙT
     Immunoassay
        (competitive, of low-mol.weight analyte, analyte-substitute reagents for)
ΙT
     Albumins, compounds
     RL: ANST (Analytical study)
        (conjugates, with cocaine analog, as immunogen for
        cocaine-reactive antibodies)
IT
     Thyroglobulins
     RL: ANST (Analytical study)
        (conjugates, with morphine analog, in morphine immunoassay)
     2321-07-5, Fluorescein
ΙT
     RL: ANST (Analytical study)
        (antibodies to, in cocaine immunoassay)
     20290-09-9D, thyroglobulin conjugates
ΙT
     RL: ANST (Analytical study)
        (as immunogen for antibodies to morphine)
IT
     57-27-2, Morphine, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (determination of, by immunoassay)
IT
     50-36-2, Cocaine
     RL: ANT (Analyte); ANST (Analytical study)
        (determination of, in urine, by competitive EIA)
IT
     140457-30-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and amination of, in cocaine analog preparation for
        immunoassay)
IT
     119094-47-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and amination of, in preparation of reagent for morphine
        immunoassay)
TΤ
     5796-31-6P, Ecgonine hydrochloride
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and esterification of, in cocaine analog preparation for
        immunoassay)
IT
     119094-63-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrogenation of, in preparation of reagent for morphine
        immunoassay)
TΤ
     140457-34-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, as cocaine analog for immunoassay)
     7143-09-1P, Ecgonine methyl ester 140457-31-4P
                                                        140457-32-5P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, in cocaine analog preparation for
        immunoassay)
     140457-34-7DP, albumin conjugates
ΙT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as immunogen, for preparation of antibodies reactive with
```

```
cocaine)
     82169-58-2DP, reaction products with morphine derivative 140476-25-1DP,
     reaction products with fluorescein derivative
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as reagent in morphine immunoassay)
ΙT
     140476-25-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, in preparation of reagent for morphine immunoassay)
     34619-03-9, Di-tert-butylcarbonate
IT
     RL: ANST (Analytical study)
        (reaction of with cocaine analog, in cocaine analog
        preparation for immunoassay)
IT
     9001-78-9D, conjugates with antibodies
     RL: ANST (Analytical study)
        (to cocaine analog, for cocaine immunoassay)
     9003-53-6D, Polystyrene, conjugates with antibodies
ΙT
     RL: ANST (Analytical study)
        (to fluorescein, in morphine immunoassay)
IT
     51306-35-5D, complexes
     RL: ANST (Analytical study)
        (with cocaine analog, as reagent for cocaine
        immunoassay)
```

```
ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
     DUPLICATE 1
AN
     1994:399497 BIOSIS
     PREV199497412497
DΝ
     Improved sensitivity of enzyme immunoassay for cocaine and
TI
     benzoylecgonine using heterologous hapten-enzyme
     conjugates.
     Chen, Peilin; Watt, David S.; Tai, Hsin-Hsiung [Reprint author]
ΑU
     Div. Med. Chem., Coll. Pharm., Univ. Ky., Lexington, KY 40536, USA
CS
     Research Communications in Substances of Abuse, (1994) Vol. 15, No. 1-2,
SO
     pp. 71-80.
     CODEN: RCSADO. ISSN: 0193-0818.
DT
     Article
     English
LA
ED
     Entered STN: 14 Sep 1994
     Last Updated on STN: 15 Sep 1994
     Antibodies for cocaine and benzoylecgonine were prepared by
     established methods using diazotized 4-aminococaine or
     4-aminobenzoylecgonine conjugated to bovine serum albumin as immunogens.
     Enzyme immunoassay was first developed using diazotized 4-aminococaine or
     4-aminobenzoylecogonine conjugated to horseradish peroxidase as the enzyme
     labels. The IC-50!s of cocaine and benzoylecgonine were 4 ng/ml
     and 2 ng/ml for their respective antibodies. However, the IC-50!s of
     cocaine and benzoylecgonine decreased to 0.4 ng/ml and 0.1 ng/ml
     respectively when two heterologous haptens, 4-formylcocaine and 4-formyl
     benzoylecgonine, were synthesized and used for enzyme labeling. The
     sensitivity of the assays was considerably improved using the heterologous
     bridge strategy.
     Biochemistry studies - General
                                      10060
CC
     Biochemistry studies - Proteins, peptides and amino acids
     Enzymes - Methods
                        10804
     Pharmacology - Neuropharmacology
                                        22024
     Toxicology - Pharmacology
     Immunology - General and methods
                                        34502
ΙT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Immune System
        (Chemical Coordination and Homeostasis); Pharmacology; Toxicology
IT
     Chemicals & Biochemicals
          COCAINE; BENZOYLECGONINE
IT
     Miscellaneous Descriptors
        ANALYTICAL METHOD; ANTIBODY CROSS-REACTIVITY; 4-AMINOBENZOYLECGONINE;
        4-AMINOCOCAINE
ORGN Classifier
                    86215
       Hominidae
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        human
     Taxa Notes
       Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN
     50-36-2 (COCAINE)
     519-09-5 (BENZOYLECGONINE)
```

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ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
     DUPLICATE 1
     1994:399497 BIOSIS
AN
     PREV199497412497
DN
ΤI
     Improved sensitivity of enzyme immunoassay for cocaine and
     benzoylecgonine using heterologous hapten-enzyme
     conjugates.
     Chen, Peilin; Watt, David S.; Tai, Hsin-Hsiung [Reprint author]
ΑU
     Div. Med. Chem., Coll. Pharm., Univ. Ky., Lexington, KY 40536, USA
CS
     Research Communications in Substances of Abuse, (1994) Vol. 15, No. 1-2,
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     pp. 71-80.
     CODEN: RCSADO. ISSN: 0193-0818.
DT
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     English
LΑ
ED
     Entered STN: 14 Sep 1994
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     Antibodies for cocaine and benzoylecgonine were prepared by
     established methods using diazotized 4-aminococaine or
     4-aminobenzoylecgonine conjugated to bovine serum albumin as immunogens.
     Enzyme immunoassay was first developed using diazotized 4-aminococaine or
     4-aminobenzoylecogonine conjugated to horseradish peroxidase as the enzyme
     labels. The IC-50!s of cocaine and benzoylecgonine were 4 ng/ml
     and 2 ng/ml for their respective antibodies. However, the IC-50!s of
     cocaine and benzoylecgonine decreased to 0.4 ng/ml and 0.1 ng/ml
     respectively when two heterologous haptens, 4-formylcocaine and 4-formyl
     benzoylecgonine, were synthesized and used for enzyme labeling. The
     sensitivity of the assays was considerably improved using the heterologous
     bridge strategy.
    Biochemistry studies - General
                                      10060
CC
     Biochemistry studies - Proteins, peptides and amino acids
     Enzymes - Methods
                        10804
     Pharmacology - Neuropharmacology
                                        22024
     Toxicology - Pharmacology
     Immunology - General and methods
                                        34502
ΙT
     Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Immune System
        (Chemical Coordination and Homeostasis); Pharmacology; Toxicology
     Chemicals & Biochemicals
IT
          COCAINE; BENZOYLECGONINE
IT
    Miscellaneous Descriptors
       ANALYTICAL METHOD; ANTIBODY CROSS-REACTIVITY; 4-AMINOBENZOYLECGONINE;
        4-AMINOCOCAINE
ORGN Classifier
       Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
       human
     Taxa Notes
       Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN
     50-36-2 (COCAINE)
     519-09-5 (BENZOYLECGONINE)
```

d his

(FILE 'HOME' ENTERED AT 12:15:04 ON 07 DEC 2004)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 12:15:23 ON 07 DEC 2004 2581 S (ENZYME CONJUGATE) L1L2 472 S L1 AND DRUG? L3 378 S L2 AND ANTIBOD? L40 S L3 AND ARRAY? L524 S L3 AND IMMOBILI? L6 22 DUPLICATE REMOVE L5 (2 DUPLICATES REMOVED) L7 6 S L1 AND COCAINE?

4 DUPLICATE REMOVE L7 (2 DUPLICATES REMOVED)

=>

L8

```
ANSWER 15 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
     1992:189194 CAPLUS
AN
     116:189194
DN
     Entered STN: 16 May 1992
ED
     Evaluation of rapid qualitative drugs of abuse kits
ΤI
     Anderson, G.; Colletti, A.; Foley, T.; Golkar, S.; Miao, R.; Patel, A.;
ΑU
     Paez, S.; Scott, M.
     Hycor Biomed. Inc., Garden Grove, CA, USA
CS
     American Clinical Laboratory (1992), 11(1), 26
SO
     CODEN: ACLAE7; ISSN: 1041-3235
DΤ
     Journal
     English
LΑ
CC
     4-2 (Toxicology)
     The accuPINCH qual. screening kits (Hycor Biomedical Inc., Garden Grove,
AΒ
     California) are easy to use and require little training and need no
     instrumentation. The test is a competitive immunoassay that incorporates
     the use of an enzyme conjugated to the resp. drug, a disk with
     antibody against the drug (separation disk), and a second
     disk containing a chromogen (detection disk). The chromogen system
     immobilized on the detection disk is ABTS in combination with
     horseradish peroxidase (HRP) and glucose. In the presence of
     enzyme conjugate, glucose is oxidized forming hydrogen
     peroxide. The latter serves as a reactant in the HRP-mediated oxidation of
     ABTS. The resulting green color is visually interpreted on the detection
     disk.
ST
     abuse drug kit evaluation; forensic abuse drug
     screening kit
IT
     Pharmaceutical analysis
        (drug screening in, forensic, screening kits in relation to)
     Legal chemistry and medicine
IT
```

(screening kits for abuse drug anal. in)

```
ANSWER 15 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
     1992:189194 CAPLUS
AN
     116:189194
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     Entered STN: 16 May 1992
ED
     Evaluation of rapid qualitative drugs of abuse kits
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     Anderson, G.; Colletti, A.; Foley, T.; Golkar, S.; Miao, R.; Patel, A.;
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     immobilized on the detection disk is ABTS in combination with
     horseradish peroxidase (HRP) and glucose. In the presence of
     enzyme conjugate, glucose is oxidized forming hydrogen
     peroxide. The latter serves as a reactant in the HRP-mediated oxidation of
     ABTS. The resulting green color is visually interpreted on the detection
     abuse drug kit evaluation; forensic abuse drug
ST
     screening kit
     Pharmaceutical analysis
IT
        (drug screening in, forensic, screening kits in relation to)
```

Legal chemistry and medicine

(screening kits for abuse drug anal. in)

IT